

In the Claims:

This listing of claims will replace all prior versions and listings of claims in the application:

1. (Previously Presented) A method for identifying nucleic acid ligands that bind to a target molecule, wherein the nucleic acid ligands comprise a 2'-OMe modified nucleotide, comprising the following steps:
 - a) preparing a transcription reaction mixture comprising a mutated polymerase, one or more 2'- modified nucleotide triphosphates (NTPs), wherein at least one NTP is a 2'-OMe NTP and at least one NTP is a 2'-OH guanosine triphosphate, magnesium ions and one or more oligonucleotide transcription templates;
 - b) preparing a candidate mixture of single-stranded nucleic acids by transcribing the one or more oligonucleotide transcription templates under conditions whereby the mutated polymerase incorporates at least one of the one or more 2'-OMe modified NTPs into nucleic acid molecules of said candidate mixture;
 - c) contacting the candidate mixture with said target molecule;
 - d) partitioning the nucleic acids having an increased affinity to the target molecule relative to the candidate mixture from the remainder of the candidate mixture; and
 - e) amplifying the increased affinity nucleic acids, in vitro, to yield a ligand-enriched mixture of nucleic acids, whereby nucleic acid ligands of the target molecule are identified.
2. - 4. (Cancelled)
5. (Original) The method of claim 1, wherein the mutated polymerase is a mutated T7 RNA polymerase.
6. (Original) The method of claim 5, wherein the mutated T7 RNA polymerase comprises a mutation at position 639 from a tyrosine residue to a phenylalanine residue (Y639F).
7. (Original) The method of claim 5, wherein the mutated T7 RNA polymerase comprises a

mutation at position 784 from a histidine residue to an alanine residue (H784A).

8. (Original) The method of claim 5, wherein the mutated T7 RNA polymerase comprises a mutation at position 639 from a tyrosine residue to a phenylalanine residue and a mutation at position 784 from a histidine residue to an alanine residue (Y639F/H784A).

9. (Original) The method of claim 1, wherein the oligonucleotide transcription template further comprises a leader sequence incorporated into a fixed region at the 5' end of the oligonucleotide transcription template.

10. (Original) The method of claim 9, wherein the leader sequence comprises an all-purine leader sequence.

11. (Original) The method of claim 10, wherein the all-purine leader sequence has a length selected from the group consisting of at least 6 nucleotides long; at least 8 nucleotides long; at least 10 nucleotides long; at least 12 nucleotides long; and at least 14 nucleotides long.

12. (Original) The method of claim 1, wherein the transcription reaction mixture further comprises manganese ions.

13. (Original) The method of claim 12, wherein the concentration of magnesium ions is between 3.0 and 3.5 times greater than the concentration of manganese ions.

14. (Previously Presented) The method of claim 1, wherein each NTP is present at a concentration of about 0.5 mM, the concentration of magnesium ions is about 5.0 mM, and the concentration of manganese ions is about 1.5 mM.

15. (Previously Presented) The method of claim 1, wherein each NTP is present at a concentration of about 1.0 mM, the concentration of magnesium ions is about 6.5 mM, and the concentration of manganese ions is about 2.0 mM.

16. (Previously Presented) The method of claim 1, wherein each NTP is present at a concentration of about 2.0 mM, the concentration of magnesium ions is about 9.6 mM, and the concentration of manganese ions is about 2.9 mM.
17. (Previously Presented) The method of claim 1, wherein the transcription reaction mixture further comprises a substituted 2'-OH guanosine or 2'-OH guanosine.
18. (Previously Presented) The method of claim 17, wherein the substituted 2'-OH guanosine is 2'-OH GMP.
19. (Previously Presented) The method of claim 1, wherein the transcription reaction mixture further comprises polyalkylene glycol.
20. (Previously Presented) The method of claim 19, wherein the polyalkylene glycol is polyethylene glycol.
21. (Previously Presented) The method of claim 1 further comprising step
f) repeating steps a) to e), wherein the one or more oligonucleotide transcription templates of step a) is a nucleic acid molecule from the ligand-enriched mixture of nucleic acids of step e).
22. - 76. (Cancelled)
77. (Previously Presented) The method of claim 1, wherein the 2'-OMe modified nucleotide triphosphates comprise a mixture of 2'-O-methyl adenosine triphosphate (ATP), 2'-O-methyl cytidine triphosphate (CTP) and 2'-O-methyl uridine triphosphate (UTP), 2'-O-methyl guanosine triphosphate (GTP) and 2'-OH guanosine triphosphate (GTP), wherein the 2'-OH guanosine triphosphate comprises a maximum of about 10% of the total guanosine triphosphate population.
78. (Previously Presented) The method of claim 1, wherein the one or more oligonucleotide

transcription templates are double stranded.

79. (Previously Presented) The method of claim 6, wherein the transcription mixture further comprises manganese ions.

80. (Previously Presented) The method of claim 79, wherein the transcription mixture further comprises 2'-OH GMP.

81. (Previously Presented) The method of claim 80, wherein the oligonucleotide transcription template further comprises an all purine leader sequence incorporated into a fixed region at the 5' end of the oligonucleotide transcription template.

82. (Previously Presented) The method of claim 81, wherein the all-purine leader sequence has a length selected from the group consisting of at least 6 nucleotides long; at least 8 nucleotides long; at least 10 nucleotides long; at least 12 nucleotides long; and at least 14 nucleotides long.

83. (Previously Presented) The method of claim 82, wherein the 2'-O-methyl modified nucleotide triphosphates comprise a mixture of 2'-adenosine triphosphate, 2'-O-methyl cytidine triphosphate, 2'-O-methyl uridine triphosphate, 2'-O-methyl guanosine triphosphate, and wherein the 2'-OH guanosine triphosphate comprises a maximum of 10% of the total guanosine triphosphate population.

84. (Previously Presented) The method of claim 83, wherein the transcription mixture further comprises spermidine or spermine.

85. (Previously Presented) The method of claim 84, wherein the transcription mixture further comprises polyethylene glycol.

86. (Previously Presented) The method of claim 85, wherein the one or more oligonucleotide

transcription templates is double stranded.

87. (Previously Presented) The method of claim 86, further comprising step f) repeating steps a) to e), wherein the one or more oligonucleotide transcription templates of step a) is a nucleic acid molecule from the ligand-enriched mixture of nucleic acids of step e).

88. (Previously Presented) The method of claim 8, wherein the transcription mixture further comprises manganese ions.

89. (Previously Presented) The method of claim 88, wherein the transcription mixture further comprises 2'-OH GMP.

90. (Previously Presented) The method of claim 89, wherein the oligonucleotide transcription template further comprises an all-purine leader sequence incorporated into a fixed region at the 5' end of the oligonucleotide transcription template.

91. (Previously Presented) The method of claim 90, wherein the all-purine leader sequence has a length selected from the group consisting of at least 6 nucleotides long; at least 8 nucleotides long; at least 10 nucleotides long; at least 12 nucleotides long; and at least 14 nucleotides long.

92. (Previously Presented) The method of claim 91, wherein the 2'-O-methyl modified nucleotide triphosphates comprise a mixture of 2'-adenosine triphosphate, 2'-O-methyl cytidine triphosphate, 2'-O-methyl uridine triphosphate, 2'-O-methyl guanosine triphosphate, and wherein the 2'-OH guanosine triphosphate comprises a maximum of about 10% of the total guanosine triphosphate population.

93. (Previously Presented) The method of claim 92, wherein the transcription mixture further comprises spermidine or spermine.

94. (Previously Presented) The method of claim 93, wherein the transcription mixture further comprises polyethylene glycol.

95. (Previously Presented) The method of claim 94, wherein the one or more oligonucleotide transcription templates is double stranded.

96. (Previously Presented) The method of claim 95, further comprising step f) repeating steps a) to e), wherein the one or more oligonucleotide transcription templates of step a) is a nucleic acid molecule from the ligand-enriched mixture of nucleic acids of step e).

97. (Withdrawn) An aptamer composition comprising a sequence where substantially all adenosine nucleotides are 2'-O-methyl adenosine, substantially all cytidine nucleotides are 2'-O-methyl cytidine, substantially all guanosine nucleotides are 2'-O-methyl guanosine or deoxy guanosine, substantially all uridine nucleotides are 2'-O-methyl uridine, wherein less than about 10% of the guanosine nucleotides are 2'-OH guanosine.

98. (Withdrawn) The aptamer composition of claim 97, wherein said aptamer comprises a sequence composition where at least 80% of all adenosine nucleotides are 2'-O-methyl adenosine, at least 80% of all cytidine nucleotides are 2'-O-methyl cytidine, at least 80% of all guanosine nucleotides are 2'-O-methyl guanosine, at least 80% of all uridine nucleotides are 2'-O-methyl uridine, and no more than about 10% of all guanosine nucleotides are 2'-OH guanosine.

99. (Withdrawn) The aptamer composition of claim 97, wherein said aptamer comprises a sequence composition where at least 90% of all adenosine nucleotides are 2'-O-methyl adenosine, at least 90% of all cytidine nucleotides are 2'-O-methyl cytidine, at least 90% of all guanosine nucleotides are 2'-O-methyl guanosine, at least 90% of all uridine nucleotides are 2'-O-methyl uridine, and no more than about 10% of all guanosine nucleotides are 2'-OH guanosine.

100. (Withdrawn) The aptamer composition of claim 97, wherein said aptamer comprises a sequence composition where 100% of all adenosine nucleotides are 2'-O-methyl adenosine, 100% of all cytidine nucleotides are 2'-O-methyl cytidine, 90% of all guanosine nucleotides are 2'-O-methyl guanosine, and 100% of all uridine nucleotides are 2'-O-methyl uridine and no more than about 10% of all guanosine nucleotides are 2'-OH guanosine.